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wherein each of said POPS blocks is flanked by a region of 2'-O-substituted ribonucleosides, and  
wherein the internucleoside linkages are selected from the group consisting of phosphodiester, phosphotriester, phosphorothioate, and phosphoramidate linkages.

#### REMARKS

Reconsideration of this application in view of the following remarks is respectfully requested. Claims 4-6 are pending in this case. Claim 4 has been amended. This amendment contains no new matter, as support can be found in the specification at page 8, lines 12-14. A marked-up copy of claim 4 is attached as Exhibit 1. A clean copy of pending claims 4-6 is attached as Exhibit 2.

Each of the rejections set forth in the Office Action dated April 20, 2001 is addressed separately below.

#### I. Rejections under 35 U.S.C. §112, Second Paragraph

Claims 4-6 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. The Examiner opines that it is unclear whether the limitation "having internucleoside linkages selected from the group consisting of phosphodiester, phosphotriester, phosphorothioate, and phosphoramidate linkages" is meant to limit the regions of 2'-O-substituted ribonucleotides or if this limitation applies to the entire oligonucleotide.

Claim 4 has been amended to recite that the limitation applies to all of the internucleoside linkages of the entire oligonucleotide, and that these linkages are selected from the group consisting of phosphodiester, phosphotriester, phosphorothioate, and phosphoramidate internucleoside linkages. Thus, applicants submit that claim 4, as amended, conveys a definite meaning to one skilled in the art.

Accordingly, Applicants respectfully submit that the rejection under 35 U.S.C. §112 is overcome and should be withdrawn.

Claims 4-6 were further rejected as being indefinite due to the recitation "one or more POPS blocks." Applicants respectfully traverse this ground of rejection.

At page 3, the Office Action states that one skilled in the art would be unable to differentiate between a single "POPS block" and a series of "one or more" contiguous "POPS blocks." The Office Action further states that one skilled in the art could not determine if "each" POPS block is flanked by regions of 2'-O-substituted ribonucleotides, or if a series of contiguous POPS blocks are flanked at each end by 2'-O-substituted ribonucleotides.

At page 6, lines 13-26 of the specification, "POPS blocks" are defined as regions of alternating phosphodiester (PO) and phosphorothioate (PS) internucleoside linkages. The specification also states that a POPS block comprises from about three to about thirty-five nucleosides (page 6, lines 27-28). Claim 4 has been amended previously to recite the limitation wherein POPS blocks are flanked by 2'-O-substituted ribonucleotides (amendment dated March 27, 2001). Thus, a region of alternating phosphodiester and phosphorothioate internucleoside linkages flanked by 2'-O-substituted ribonucleotides constitutes a single POPS block, not a series of contiguous POPS blocks, whether it is three or thirty-five nucleosides in length. Applicants submit that one of skill in the art would understand that the entire region of nucleotides characterized by alternating phosphodiester and phosphorothioate internucleoside linkages and flanked by 2'-O-substituted ribonucleotides constitutes a single POPS block.

Accordingly, Applicants respectfully request that the rejection of claims 4-6 under 35 U.S.C. §112, second paragraph, be reconsidered and withdrawn.

II. Rejections under 35 U.S.C. §102 (b)

Claims 4-6 stand rejected under 35 U.S.C. §102 (b) as being anticipated by Arnold et al.

Claims 4-6 are directed to oligonucleotides comprising regions of alternating phosphodiester and phosphorothioate internucleoside linkages termed "POPS blocks," which are flanked by regions of 2'-O-substituted ribonucleotides. Independent claim 4, as amended, is drawn to oligonucleotides wherein all of the internucleoside linkages are selected from the group consisting of phosphodiester, phosphotriester, phosphorothioate, and phosphoramidate internucleoside linkages. The open language to which the Examiner objected has been amended, such that other internucleoside linkages, such as methylphosphonate linkages, are clearly excluded. Dependent claims 5 and 6 likewise contain such a limitation.

Arnold et al. teaches oligonucleotides comprising regions of methylphosphonate internucleoside linkages at the 3' and 5' termini. Arnold et al. does not teach or suggest oligonucleotides with regions of alternating phosphodiester and phosphorothioate internucleoside linkages which do not also contain regions of methylphosphonate internucleoside linkages at the 3' and 5' termini. Thus, Arnold et al. does not teach the invention as required by amended claim 4.

Thus, Applicants aver that amended claim 4 and claims 5-6 dependent thereon, satisfy the requirements of 35 U.S.C. §102(b). Accordingly, Applicants respectfully request that the rejection of claims 4-6 under 35 U.S.C. §102(b) be reconsidered and withdrawn.

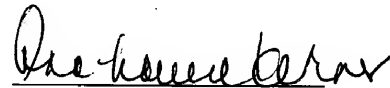
CONCLUSIONS

Applicants posit the rejections contained in the Office Action dated April 20, 2001 have been overcome by amendment or argument. Therefore, reconsideration of this application and its allowance are respectfully requested.

No fee is believed due at this time. However, please charge any fees or credit any overpayments to our Deposit Account No. 08-0219.

The Examiner is encouraged to call the undersigned to expedite prosecution.

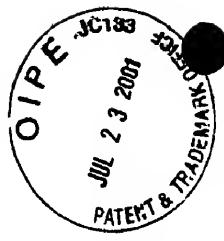
Respectfully submitted,  
HALE AND DORR LLP



Ann-Louise Kerner, Ph.D.  
Registration No. 33,523  
Attorney for Applicants

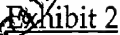
July 19, 2001  
60 State Street  
Boston, MA 02109  
(617) 526-6000  
(617) 526-5000 (fax)

Exhibit 1



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4. (Amended) A hybrid oligonucleotide consisting of one or more deoxyribonucleotide POPS blocks and one or more regions of 2'-O-substituted ribonucleotides [having internucleoside linkages selected from the group consisting of phosphodiester, phosphotriester, phosphorothioate, and phosphoramidate linkages], wherein each of said POPS blocks is flanked by a region of 2'-O-substituted ribonucleosides, and
- wherein the internucleoside linkages are selected from the group consisting of phosphodiester, phosphotriester, phosphorothioate, and phosphoramidate linkages.



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